Synthesis of (±)-Deoxybruceol

Syntheses and Some Properties of 2- and 6-Hydroxyazulenes

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HYDROXYAZULENES are of interest as hydroxy-derivatives of bicyclic nonbenzenoid aromatic compounds isomeric with the naphthols. In our laboratory,[1] various 2-hydroxyazulene derivatives with alkoxycarbonyl and/or cyano-groups have been synthesized. Hafner *et al.* reported the synthesis of 6-hydroxy-4,8-dimethylazulene,[2] and Chiurdoglu *et al.* reported that 3-hydroxyguaiazulene was synthesized from 3-formylguaiazulene and existed only in its keto-form.[3] Recently, Heilbronner synthesized 2-hydroxyguaiazulene from guaiazulene-2-sulphonic acid, and studied its keto–enol tautomerism in various solvents.[4] However, none of the parent hydroxyazulenes, for which five isomers would be expected, has been obtained, except possibly 4-hydroxyazulene.[5]

We now report on the syntheses of 2- and 6-hydroxyazulenes, together with some of their chemical and physical properties.

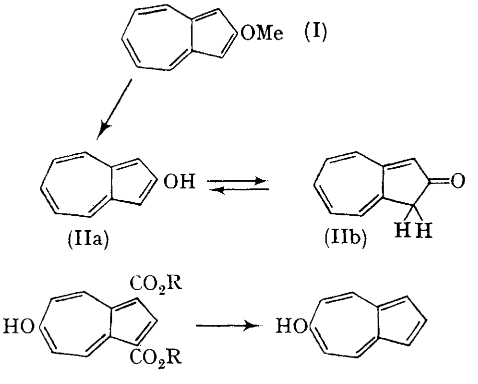
Hydrolysis of 2-methoxyazulene (I)[6] with 48% hydrobromic acid at 90° afforded 2-hydroxyazulene (II), m.p. 115·5—116·5°, as reddish plates (yield 90%). The same compound (II) was also obtained, in 45% yield, by treating diethyl or dimethyl

2-hydroxyazulene-1,3-dicarboxylate[6b] with 48% hydrobromic acid; however, similar treatment of these esters with anhydrous phosphoric acid afforded (II) in low yield, together with 2-ethoxy- or 2-methoxy-azulene in about 40% yield.

Dealkoxycarbonylation of diethyl or dimethyl 6-hydroxyazulene-1,3-dicarboxylate (III)[7] was effected by heating with anhydrous phosphoric acid at 90° for 2 hr. to give 6-hydroxyazulene (IV), m.p. 126—127° as reddish plates in 40% yield.

The compound (II) is stable in air at room temperature; however, the compound (IV) is gradually converted into a black resin under the same conditions. The compound (II) gave 2-methoxy-[6] and 2-ethoxy-azulene[6] by reaction with diazomethane and diazoethane, respectively, or with the corresponding alcohols in the presence of phosphoric acid, and also gave the acetate, m.p. 55—65°. The compound (IV) also afforded 6-methoxy-,[8] m.p. 112—113°; 6-ethoxy-, m.p. 80—81°; 6-acetoxy-, m.p. 118—119°; and 6-benzoyloxy-azulene, m.p. 162—163°.

The pK_a values of 2- and 6-hydroxyazulenes in water (measured by the u.v.-spectral method) are 8·71 and 7·38, respectively, [*cf.* phenol (pK_a, 9·94), α-naphthol (9·23)].



(I)

(IIa) (IIb)

(III) R=Me or Et (IV)

The u.v. spectrum (Figure) of (II) in methanol shows a curve typical of azulene derivatives; however, the spectra in chloroform and in water are quite different from that in methanol and similar to those of 1-oxa-azulen-2-one[9] and diethyl 1-bromo-2(1*H*)-oxoazulene-1,3-dicarboxylate[10] in methanol. The i.r. spectrum of (II) (KBr disc) shows no carbonyl band, though the spectrum in chloroform solution shows a strong band at 1642 cm.$^{-1}$. These results indicate the existence of tautomerism between 2-hydroxyazulene (IIa) and 2(1*H*)-azulenone (IIb) in compound (II).

The n.m.r. spectrum of (II) in $(CD_3)_2CO$ or in $(CD_3)_2SO$ shows a similar pattern to that of 2-methoxyazulene in $CDCl_3$, however, the spectrum of (II) in $CDCl_3$ exhibits additional peaks to that in $(CD_3)_2CO$ between 6·7 and 3·0 p.p.m. Furthermore, the singlets at 3·07, 5·80,† and 6·86 p.p.m. in $CDCl_3$ gradually disappeared on addition of D_2O and a peak due to water protons appeared at 4·6 p.p.m.

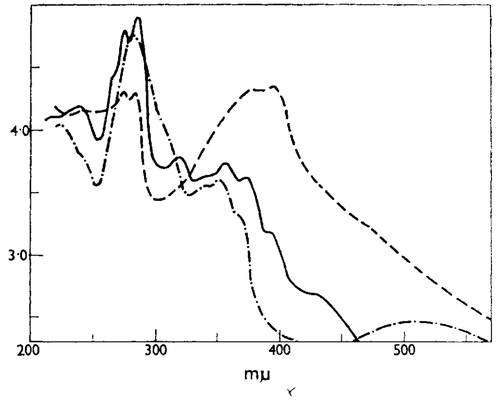


FIGURE. *Ultraviolet spectra of* (II) *in methanol* (—), *in water* (— — —), *and of* (IV) *in methanol* (—·—·).

These observations also confirmed the existence of solvent-dependent tautomerism in compound (II) (*cf.* 2-hydroxyguaiazulene[4]).

The apparent enol–keto ratios in various solvents calculated from the intensities of u.v. absorption at 284 mμ are shown in the Table, on the assumption that the apparent extinction coefficient at 284 mμ in methanol is representative of the extinction coefficient of the enol tautomer.

TABLE

Apparent enol–keto ratios (K_e)

Solvent	ε*(at 284 mμ)	K_e
Methanol	74,300	(∞)
Dioxan	70,100	16·7
Me_2SO	70,000	16·3
DMF	58,000	3·56
Iso-octane	45,000	1·54
50% Methanol	34,200	0·85
Ether	22,400	0·43
CCl_4	17,800	0·31
H_2O	14,900	0·25
$CHCl_3$	6,070	0·09

* Apparent extinction coefficient of enol form (IIa).

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† The chemical shift of H-3 of (IIb) was assigned by analogy with that of 1-oxa-azulane-2-one, 5·79 p.p.m.; unpublished datum in our laboratory.

On the other hand, u.v., i.r., and n.m.r. spectra of 6-hydroxyazulene (IV) are similar to those of 6-methoxyazulene and do not change with different solvents, therefore, the compound (IV) must exist only as its enol form.

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